

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

Date of mailing (day/month/year) 17 October 2000 (17.10.00)	in its capacity as elected Office
International application No. PCT/GB00/00912	Applicant's or agent's file reference PHM.70514/WO
International filing date (day/month/year) 13 March 2000 (13.03.00)	Priority date (day/month/year) 17 March 1999 (17.03.99)
Applicant BROWN, Dearg, Sutherland	

1. The designated Office is hereby notified of its election made:

in the demand filed with the International Preliminary Examining Authority on:

19 September 2000 (19.09.00)

in a notice effecting later election filed with the International Bureau on:

2. The election was

was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

<p>The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland</p> <p>Facsimile No.: (41-22) 740.14.35</p>	<p>Authorized officer</p> <p>S. Mafia</p> <p>Telephone No.: (41-22) 338.83.38</p>
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09/936758

PCT

REQUEST

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.

For receiving Office use only

International Application No.

International Filing Date

Name of receiving Office and "PCT International Application"

Applicant's or agent's file reference
(if desired) (12 characters maximum) PHM.70514/WO

Box No. I TITLE OF INVENTION

AMIDE DERIVATIVES

Box No. II APPLICANT

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

ASTRAZENECA UK Limited
15 Stanhope Gate
London. W1Y 6LN
GB.

 This person is also inventor.

Telephone No.

(01625) 516173

Facsimile No.

(01625) 583358

Teleprinter No.

State (that is, country) of nationality:
GBState (that is, country) of residence:
GB

This person is applicant all designated States all designated States except the United States of America the United States of America only the States indicated in the Supplemental Box

Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

BROWN, Dearg Sutherland
ASTRAZENECA
Mereside, Alderley Park,
Macclesfield, Cheshire. SK10 4TG.
GB

This person is:

 applicant only applicant and inventor inventor only (If this check-box is marked, do not fill in below.)State (that is, country) of nationality:
GBState (that is, country) of residence:
GB

This person is applicant all designated States all designated States except the United States of America the United States of America only the States indicated in the Supplemental Box

 Further applicants and/or (further) inventors are indicated on a continuation sheet.

Box No. IV AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE

The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as:

 agent common representative

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)

TAIT, Brian Steele
ASTRAZENECA
Mereside, Alderley Park,
Macclesfield, Cheshire. SK10 4TG.
GB.

Telephone No.

(01625) 514151

Facsimile No.

(01625) 583358

Teleprinter No.

Address for correspondence: Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.

Box No.V DESIGNATION OF STATES

The following designations are hereby made under Rule 4.9(a) (*mark the applicable check-boxes; at least one must be marked*):

Regional Patent

- AP ARIPO Patent:** **GH** Ghana, **GM** Gambia, **KE** Kenya, **LS** Lesotho, **MW** Malawi, **SD** Sudan, **SL** Sierra Leone, **SZ** Swaziland, **TZ** United Republic of Tanzania, **UG** Uganda, **ZW** Zimbabwe, and any other State which is a Contracting State of the Harare Protocol and of the PCT
- EA Eurasian Patent:** **AM** Armenia, **AZ** Azerbaijan, **BY** Belarus, **KG** Kyrgyzstan, **KZ** Kazakhstan, **MD** Republic of Moldova, **RU** Russian Federation, **TJ** Tajikistan, **TM** Turkmenistan, and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT
- EP European Patent:** **AT** Austria, **BE** Belgium, **CH and LI** Switzerland and Liechtenstein, **CY** Cyprus, **DE** Germany, **DK** Denmark, **ES** Spain, **FI** Finland, **FR** France, **GB** United Kingdom, **GR** Greece, **IE** Ireland, **IT** Italy, **LU** Luxembourg, **MC** Monaco, **NL** Netherlands, **PT** Portugal, **SE** Sweden, and any other State which is a Contracting State of the European Patent Convention and of the PCT
- OA OAPI Patent:** **BF** Burkina Faso, **BJ** Benin, **CF** Central African Republic, **CG** Congo, **CI** Côte d'Ivoire, **CM** Cameroon, **GA** Gabon, **GN** Guinea, **GW** Guinea-Bissau, **ML** Mali, **MR** Mauritania, **NE** Niger, **SN** Senegal, **TD** Chad, **TG** Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT (*if other kind of protection or treatment desired, specify on dotted line*)

National Patent (if other kind of protection or treatment desired, specify on dotted line):

- | | |
|---|---|
| <input checked="" type="checkbox"/> AE United Arab Emirates | <input checked="" type="checkbox"/> LR Liberia |
| <input checked="" type="checkbox"/> AL Albania | <input checked="" type="checkbox"/> LS Lesotho |
| <input checked="" type="checkbox"/> AM Armenia | <input checked="" type="checkbox"/> LT Lithuania |
| <input checked="" type="checkbox"/> AT Austria | <input checked="" type="checkbox"/> LU Luxembourg |
| <input checked="" type="checkbox"/> AU Australia | <input checked="" type="checkbox"/> LV Latvia |
| <input checked="" type="checkbox"/> AZ Azerbaijan | <input checked="" type="checkbox"/> MA Morocco |
| <input checked="" type="checkbox"/> BA Bosnia and Herzegovina | <input checked="" type="checkbox"/> MD Republic of Moldova |
| <input checked="" type="checkbox"/> BB Barbados | <input checked="" type="checkbox"/> MG Madagascar |
| <input checked="" type="checkbox"/> BG Bulgaria | <input checked="" type="checkbox"/> MK The former Yugoslav Republic of Macedonia |
| <input checked="" type="checkbox"/> BR Brazil | <input checked="" type="checkbox"/> MN Mongolia |
| <input checked="" type="checkbox"/> BY Belarus | <input checked="" type="checkbox"/> MW Malawi |
| <input checked="" type="checkbox"/> CA Canada | <input checked="" type="checkbox"/> MX Mexico |
| <input checked="" type="checkbox"/> CH and LI Switzerland and Liechtenstein | <input checked="" type="checkbox"/> NO Norway |
| <input checked="" type="checkbox"/> CN China | <input checked="" type="checkbox"/> NZ New Zealand |
| <input checked="" type="checkbox"/> CR Costa Rica | <input checked="" type="checkbox"/> PL Poland |
| <input checked="" type="checkbox"/> CU Cuba | <input checked="" type="checkbox"/> PT Portugal |
| <input checked="" type="checkbox"/> CZ Czech Republic | <input checked="" type="checkbox"/> RO Romania |
| <input checked="" type="checkbox"/> DE Germany | <input checked="" type="checkbox"/> RU Russian Federation |
| <input checked="" type="checkbox"/> DK Denmark | <input checked="" type="checkbox"/> SD Sudan |
| <input checked="" type="checkbox"/> DM Dominica | <input checked="" type="checkbox"/> SE Sweden |
| <input checked="" type="checkbox"/> EE Estonia | <input checked="" type="checkbox"/> SG Singapore |
| <input checked="" type="checkbox"/> ES Spain | <input checked="" type="checkbox"/> SI Slovenia |
| <input checked="" type="checkbox"/> FI Finland | <input checked="" type="checkbox"/> SK Slovakia |
| <input checked="" type="checkbox"/> GB United Kingdom | <input checked="" type="checkbox"/> SL Sierra Leone |
| <input checked="" type="checkbox"/> GD Grenada | <input checked="" type="checkbox"/> TJ Tajikistan |
| <input checked="" type="checkbox"/> GE Georgia | <input checked="" type="checkbox"/> TM Turkmenistan |
| <input checked="" type="checkbox"/> GH Ghana | <input checked="" type="checkbox"/> TR Turkey |
| <input checked="" type="checkbox"/> GM Gambia | <input checked="" type="checkbox"/> TT Trinidad and Tobago |
| <input checked="" type="checkbox"/> HR Croatia | <input checked="" type="checkbox"/> TZ United Republic of Tanzania |
| <input checked="" type="checkbox"/> HU Hungary | <input checked="" type="checkbox"/> UA Ukraine |
| <input checked="" type="checkbox"/> ID Indonesia | <input checked="" type="checkbox"/> UG Uganda |
| <input checked="" type="checkbox"/> IL Israel | <input checked="" type="checkbox"/> US United States of America |
| <input checked="" type="checkbox"/> IN India | <input checked="" type="checkbox"/> UZ Uzbekistan |
| <input checked="" type="checkbox"/> IS Iceland | <input checked="" type="checkbox"/> VN Viet Nam |
| <input checked="" type="checkbox"/> JP Japan | <input checked="" type="checkbox"/> YU Yugoslavia |
| <input checked="" type="checkbox"/> KE Kenya | <input checked="" type="checkbox"/> ZA South Africa |
| <input checked="" type="checkbox"/> KG Kyrgyzstan | <input checked="" type="checkbox"/> ZW Zimbabwe |
| <input checked="" type="checkbox"/> KP Democratic People's Republic of Korea | |
| <input checked="" type="checkbox"/> KR Republic of Korea | |
| <input checked="" type="checkbox"/> KZ Kazakhstan | |
| <input checked="" type="checkbox"/> LC Saint Lucia | |
| <input checked="" type="checkbox"/> LK Sri Lanka | |

Check-boxes reserved for designating States which have become party to the PCT after issuance of this sheet:

- DZ** Algeria
 AG Antigua

Precautionary Designation Statement: In addition to the designations made above, the applicant also makes under Rule 4.9(b) all other designations which would be permitted under the PCT except any designation(s) indicated in the Supplemental Box as being excluded from the scope of this statement. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. (*Confirmation (including fees) must reach the receiving Office within the 15-month time limit*)

Box No. VI PRIORITY CLAIM		<input type="checkbox"/> Further priority claims are indicated in the Supplemental Box.		
Filing date of earlier application (day/month/year)	Number of earlier application	Where earlier application is:		
		national application: country	regional application: regional Office	international application: receiving Office
item (1) 17MAR1999 17/03/99	9906279.6	GB		
item (2) 11NOV1999 11/11/99	9926667.8	GB		
item (3)				

The receiving Office is requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) (only if the earlier application was filed with the Office which for the purposes of the present international application is the receiving Office) identified above as item(s).

* Where the earlier application is an ARIPO application, it is mandatory to indicate in the Supplemental Box at least one country party to the Paris Convention for the Protection of Industrial Property for which that earlier application was filed (Rule 4.10(b)(ii)). See Supplemental Box.

Box No. VII INTERNATIONAL SEARCHING AUTHORITY

Choice of International Searching Authority (ISA)
(if two or more International Searching Authorities are competent to carry out the international search, indicate the Authority chosen; the two-letter code may be used):

ISA /

Request to use results of earlier search; reference to that search (if an earlier search has been carried out by or requested from the International Searching Authority):
Date (day/month/year) Number Country (or regional Office)

Box No. VIII CHECK LIST; LANGUAGE OF FILING

This international application contains the following number of sheets:

request : 03

description (excluding sequence listing part) : 120

claims : 19

abstract : 01

drawings :

sequence listing part of description :

Total number of sheets : 143

This international application is accompanied by the item(s) marked below:

1. fee calculation sheet
2. separate signed power of attorney
3. copy of general power of attorney; reference number, if any:
4. statement explaining lack of signature
5. priority document(s) identified in Box No. VI as item(s):
6. translation of international application into (language):
7. separate indications concerning deposited microorganism or other biological material
8. nucleotide and/or amino acid sequence listing in computer readable form
9. other (specify):

Figure of the drawings which should accompany the abstract:

Language of filing of the international application: ENGLISH

Box No. IX SIGNATURE OF APPLICANT OR AGENT

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the request).

TAIT, Brian Steele
AGENT FOR APPLICANT

For receiving Office use only		
1. Date of actual receipt of the purported international application:	2. Drawings:	
3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application:	<input type="checkbox"/> received:	
4. Date of timely receipt of the required corrections under PCT Article 11(2):	<input type="checkbox"/> not received:	
5. International Searching Authority (if two or more are competent): ISA /	6. <input type="checkbox"/> Transmittal of search copy delayed until search fee is paid.	

For International Bureau use only	
Date of receipt of the record copy by the International Bureau:	

This sheet is not part of and does not count as a sheet of the international application.

PCT

FEE CALCULATION SHEET Annex to the Request

For receiving Office use only

International application No.

Date stamp of the receiving Office

Applicant's or agent's file reference PHM.70514/WO

Applicant ASTRAZENECA UK Limited

CALCULATION OF PRESCRIBED FEES

1. TRANSMITTAL FEE 55.00 T

2. SEARCH FEE 638.00 S

International search to be carried out by _____

(If two or more International Searching Authorities are competent in relation to the international application, indicate the name of the Authority which is chosen to carry out the international search.)

3. INTERNATIONAL FEE

Basic Fee

The international application contains 143 sheets.

first 30 sheets 264.00 b1
 $113 \times 6.00 = 678.00$ b2

remaining sheets additional amount

Add amounts entered at b1 and b2 and enter total at B 942.00 B

Designation Fees 85

The international application contains _____ designations.

$8 \times 56.00 = 448.00$ D

number of designation fees amount of designation fee
payable (maximum 8)

1390.00 I

Add amounts entered at B and D and enter total at I

(Applicants from certain States are entitled to a reduction of 75% of the international fee. Where the applicant is (or all applicants are) so entitled, the total to be entered at I is 25% of the sum of the amounts entered at B and D.)

4. FEE FOR PRIORITY DOCUMENT (if applicable) P

5. TOTAL FEES PAYABLE 2083.00

Add amounts entered at T, S, I and P, and enter total in the TOTAL box

TOTAL

The designation fees are not paid at this time.

MODE OF PAYMENT

authorization to charge
deposit account (see below)

bank draft

coupons

cheque

cash

other (specify): _____

postal money order

revenue stamps

DEPOSIT ACCOUNT AUTHORIZATION (this mode of payment may not be available at all receiving Offices)

The RO/ is hereby authorized to charge the total fees indicated above to my deposit account.

(this check-box may be marked only if the conditions for deposit accounts of the receiving Office so permit) is hereby authorized to charge any deficiency or credit any overpayment in the total fees indicated above to my deposit account.

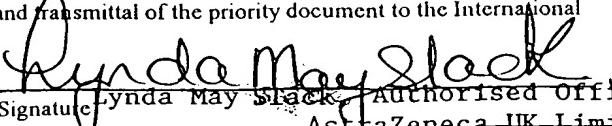
is hereby authorized to charge the fee for preparation and transmittal of the priority document to the International Bureau of WIPO to my deposit account.

D02934

10-Mar-00

Deposit Account No.

Date (day/month/year)


Signature: Lynda May Slack Authorised Officer
AstraZeneca UK Limited

PATENT COOPERATION TREATY

From the RECEIVING OFFICE

To:

PCT

**NOTIFICATION REGARDING CERTAIN
CORRECTIONS MADE *EX OFFICIO***

(PCT Administrative Instructions, Section 327)

		Date of mailing (day/month/year) 20. 3. 2000
Applicant's or agent's file reference PHM. 70514. WO	REPLY DUE	NONE However, see paragraph 3 below
International application No. PCT/GB 00/00912	International filing date (day/month/year)	13. 3. 2000
Applicant AstraZeneca UK Ltd.		

1. The applicant is hereby notified that this receiving Office has corrected formal defects in the international application *ex officio*, as shown on the attached copy of:

the request, sheet No.: Page 2
 the description, sheet No.: _____
 the claims, sheet No.: _____
 the drawings, sheet No.: _____
 other (specify): _____

2. If the applicant agrees with these corrections, no further action is required in this regard.
3. In case of disagreement with these corrections, the applicant should promptly inform this receiving Office accordingly.

Name and mailing address of the receiving Office The Patent Office Cardiff Road, Newport South Wales NP9 1RH Facsimile No.	Authorized officer P. J. TREEN ROOM: GY9 EXT: 4340 Telephone No.
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Box No.V DESIGNATION OF STATES

The following designations are hereby made under Rule 4.9(a) (mark the applicable check-boxes; at least one must be marked):

Regional Patent

- AP ARIPO Patent: GHhana, GM Gambia, KE Kenya, LS Lesotho, MW Malawi, SD Sudan, SL Sierra Leone, SZ Swaziland, TZ United Republic of Tanzania, UG Uganda, ZW Zimbabwe, and any other State which is a Contracting State of the Harare Protocol and of the PCT
- EA Eurasian Patent: AMmenia, AZAzerbaijan, BY Belarus, KG Kyrgyzstan, KZKazakhstan, MD Republic of Moldova, RU Russian Federation, TJ Tajikistan, TM Turkmenistan, and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT
- EP European Patent: AT Austria, BE Belgium, CH and LSwitzerland and Liechtenstein, CY Cyprus, DE Germany, DK Denmark, ESSpain, FIFinland, FRFrance, GB United Kingdom, GRGreece, IE Ireland, IT Italy, LU Luxembourg, MC Monaco, NL Netherlands, PT Portugal, SE Sweden, and any other State which is a Contracting State of the European Patent Convention and of the PCT
- OA OAPI Patent: BBurkina Faso, BJ Benin, CF Central African Republic, CG Congo, CI Côte d'Ivoire, CM Cameroons, GA Gabon, GN Guinea, GW Guinea-Bissau, MLMali, MR Mauritania, NE Niger, SN Senegal, TD Chad, TG Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT (if other kind of protection or treatment desired, specify on dotted line)

National Patent(if other kind of protection or treatment desired, specify on dotted line):

- | | |
|--|--|
| <input checked="" type="checkbox"/> AE United Arab Emirates | <input checked="" type="checkbox"/> LR Liberia |
| <input checked="" type="checkbox"/> AL Albania | <input checked="" type="checkbox"/> LS Lesotho |
| <input checked="" type="checkbox"/> AM Armenia | <input checked="" type="checkbox"/> LT Lithuania |
| <input checked="" type="checkbox"/> AT Austria | <input checked="" type="checkbox"/> LU Luxembourg |
| <input checked="" type="checkbox"/> AU Australia | <input checked="" type="checkbox"/> LV Latvia |
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| <input checked="" type="checkbox"/> BG Bulgaria | <input checked="" type="checkbox"/> MK The former Yugoslav Republic of Macedonia |
| <input checked="" type="checkbox"/> BR Brazil | <input checked="" type="checkbox"/> MN Mongolia |
| <input checked="" type="checkbox"/> BY Belarus | <input checked="" type="checkbox"/> MW Malawi |
| <input checked="" type="checkbox"/> CA Canada | <input checked="" type="checkbox"/> MX Mexico |
| <input checked="" type="checkbox"/> CH and LSwitzerland and Liechtenstein | <input checked="" type="checkbox"/> NO Norway |
| <input checked="" type="checkbox"/> CN China | <input checked="" type="checkbox"/> NZ New Zealand |
| <input checked="" type="checkbox"/> CR Costa Rica | <input checked="" type="checkbox"/> PL Poland |
| <input checked="" type="checkbox"/> CU Cuba | <input checked="" type="checkbox"/> PT Portugal |
| <input checked="" type="checkbox"/> CZ Czech Republic | <input checked="" type="checkbox"/> RO Romania |
| <input checked="" type="checkbox"/> DE Germany | <input checked="" type="checkbox"/> RU Russian Federation |
| <input checked="" type="checkbox"/> DK Denmark | <input checked="" type="checkbox"/> SD Sudan |
| <input checked="" type="checkbox"/> DM Dominica | <input checked="" type="checkbox"/> SE Sweden |
| <input checked="" type="checkbox"/> EE Estonia | <input checked="" type="checkbox"/> SG Singapore |
| <input checked="" type="checkbox"/> ES Spain | <input checked="" type="checkbox"/> SI Slovenia |
| <input checked="" type="checkbox"/> FI Finland | <input checked="" type="checkbox"/> SK Slovakia |
| <input checked="" type="checkbox"/> GB United Kingdom | <input checked="" type="checkbox"/> SL Sierra Leone |
| <input checked="" type="checkbox"/> GD Grenada | <input checked="" type="checkbox"/> TJ Tajikistan |
| <input checked="" type="checkbox"/> GE Georgia | <input checked="" type="checkbox"/> TM Turkmenistan |
| <input checked="" type="checkbox"/> GH Ghana | <input checked="" type="checkbox"/> TR Turkey |
| <input checked="" type="checkbox"/> GM Gambia | <input checked="" type="checkbox"/> TT Trinidad and Tobago |
| <input checked="" type="checkbox"/> HR Croatia | <input checked="" type="checkbox"/> TZ United Republic of Tanzania |
| <input checked="" type="checkbox"/> HU Hungary | <input checked="" type="checkbox"/> UA Ukraine |
| <input checked="" type="checkbox"/> ID Indonesia | <input checked="" type="checkbox"/> UG Uganda |
| <input checked="" type="checkbox"/> IL Israel | <input checked="" type="checkbox"/> US United States of America |
| <input checked="" type="checkbox"/> IN India | <input checked="" type="checkbox"/> UZ Uzbekistan |
| <input checked="" type="checkbox"/> IS Iceland | <input checked="" type="checkbox"/> VN Viet Nam |
| <input checked="" type="checkbox"/> JP Japan | <input checked="" type="checkbox"/> YU Yugoslavia |
| <input checked="" type="checkbox"/> KE Kenya | <input checked="" type="checkbox"/> ZA South Africa |
| <input checked="" type="checkbox"/> KG Kyrgyzstan | <input checked="" type="checkbox"/> ZW Zimbabwe |
| <input checked="" type="checkbox"/> KP Democratic People's Republic of Korea | Check-boxes reserved for designating States which have become party to the PCT after issuance of this sheet: |
| <input checked="" type="checkbox"/> KR Republic of Korea | <input checked="" type="checkbox"/> DZ Algeria |
| <input checked="" type="checkbox"/> KZ Kazakhstan | <input checked="" type="checkbox"/> AG Antigua |
| <input checked="" type="checkbox"/> LC Saint Lucia | |
| <input checked="" type="checkbox"/> LK Sri Lanka | |

Precautionary Designation Statement In addition to the designations made above, the applicant also makes under Rule 4.9(b) all other designations which would be permitted under the PCT except any designation(s) indicated in the Supplemental Box as being excluded from the scope of this statement. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. (Confirmation (including fees) must reach the receiving Office within the 15-month time limit.)

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PATENT COOPERATION TREATY

REC'D C2 APR 2001

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference PHM.70514/WO	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/GB00/00912	International filing date (day/month/year) 13/03/2000	Priority date (day/month/year) 17/03/1999
International Patent Classification (IPC) or national classification and IPC C07D401/12		
Applicant ASTRAZENECA UK LIMITED et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 7 sheets, including this cover sheet.

This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I Basis of the report
- II Priority
- III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV Lack of unity of invention
- V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI Certain documents cited
- VII Certain defects in the international application
- VIII Certain observations on the international application

Date of submission of the demand 19/09/2000	Date of completion of this report 29.03.2001
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Scruton-Evans, I Telephone No. +49 89 2399 8272



**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/GB00/00912

I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17.)*):

Description, pages:

1-120 as originally filed

Claims, No.:

1-12 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- the language of publication of the international application (under Rule 48.3(b)).
- the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- contained in the international application in written form.
- filed together with the international application in computer readable form.
- furnished subsequently to this Authority in written form.
- furnished subsequently to this Authority in computer readable form.
- The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- the description, pages:
- the claims, Nos.:
- the drawings, sheets:

5. This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/GB00/00912

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:
- the entire international application.
- claims Nos. 12.

because:

- the said international application, or the said claims Nos. 12 relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet
- the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- no international search report has been established for the said claims Nos. .
2. A meaningful international preliminary examination report cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:
- the written form has not been furnished or does not comply with the standard.
- the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N) Yes: Claims 1-12
 No: Claims

Inventive step (IS) Yes: Claims 1-12
 No: Claims

Industrial applicability (IA) Yes: Claims 1-11

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/GB00/00912

No: Claims

2. Citations and explanations
see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet



**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/GB00/00912

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claim 12 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of this claim (Article 34(4)(a)(i) PCT).

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

The following documents cited in the Search Report are referred to in this communication;

- D1: Chem. Abs. 077: 019599 (17-07-1972),
Izv. Vyssh. Ucheb. Zaved., Khim. Khim. Tekhnol. (ivukar);1971; Vol.14 (11); Pp.1685-9 (0000), , -
- D2: Chem. Abs. 069: 059182 (07-10-1968),
Can. J. Chem. (cjchag);1968; Vol.46 (15); Pp.2519-24 (0000), , -
- D3: Expert Opinion On Therapeutic Patents,gb,ashley Publications (01-01-1997), 7(7), 729-733
- D4: WO-A-0007991
- D5: WO-A-9535304

Document D4 was published after the priority date of the present application, and thus its relevance cannot be assessed until such a time as the priority of the present application has been studied.

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/GB00/00912

With regard to the requirement for novelty (Article 33(2) of the PCT), the compounds disclosed in D1 are excluded from the compound claims 1 and 2, and no pharmaceutical use is disclosed therein, and thus novelty of claims 10 and 11 re D1 is established. Document D2 discloses compound differing in their hydrazide group, and those of D3, a general article, are not quinazoline derivatives. D5 discloses pyrimidine and purine derivatives, which differ structurally. Article 33(2) of the PCT thus appears to have been satisfied.

The compounds of the present application are described as being cytokine inhibitors. The prior arts D3 and D5 both disclose such an activity. The man skilled in the art, faced with the problem of providing further novel compounds with this qualitative activity would not have necessarily arrived at the compounds of the present application as they are structurally distinct from those known to have the same activity. Thus in principle, for those compounds actually shown to have been active, i.e. to have solved the problem, Article 33(3) of the PCT could be considered to be satisfied.

For the use of the terms "aryl", "heteroaryl" etc without further specification within the claims as to their exact meaning , the arguments put forward in your reply as to why they are justified and the statement made therein that it is reasonable to expect that all will possess the required cytokine inhibitory activity have been considered and do appear to justify a broad scope for the claim. However, whether this breadth can include such terms as heteroaryl without any limitation on the size or nature of the ring, the number of the rings or indeed the heteroatom included is still considered to be speculative, and it is contended that an unambiguous supported definition would be that as in the description wherein the size and nature of the heteroatoms is included. For the assessment of the present claim 12 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/GB00/00912

Re Item VII

Certain defects in the international application

It is not clear why claims 1 and 2 have been formulated as independent claims, the only apparent difference being the absence of the oxo or thioxo substituent possibility in claim 2 and the specification of X as NHCO. The claim 2 should be dependent on claim 1 (Rule 6.4a) of the PCT).

The term "in-vivo cleavable ester" is objected to as being a functional definition, whose actual scope is not clear without performing in-vivo tests to ascertain which esters fall within this category, which places an undue burden on the reader of the application.

PATENT COOPERATION TREATY

PCT

091936758

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference PHM. 70514/WO	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/GB 00/00912	International filing date (<i>day/month/year</i>) 13/03/2000	(Earliest) Priority Date (<i>day/month/year</i>) 17/03/1999
Applicant ASTRAZENECA UK LIMITED et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

- the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :
- contained in the international application in written form.
 - filed together with the international application in computer readable form.
 - furnished subsequently to this Authority in written form.
 - furnished subsequently to this Authority in computer readable form.
 - the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
 - the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. **Certain claims were found unsearchable** (See Box I).

3. **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

- the text is approved as submitted by the applicant.
- the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

- the text is approved as submitted by the applicant.
- the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

- as suggested by the applicant.
- because the applicant failed to suggest a figure.
- because this figure better characterizes the invention.

_____ None of the figures.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB 00/00912

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:

Although claim 12 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
- No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 00/00912

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7	C07D401/12	C07D239/96	C07D239/91	C07D403/12	C07D405/12
	C07D409/12	C07D409/14	C07D405/14	A61K31/505	A61P43/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>CHEMICAL ABSTRACTS, vol. 077, no. 3, 17 July 1972 (1972-07-17) Columbus, Ohio, US; abstract no. 019599, KOZHEVNIKOV Y V: "Synthesis of nitro and amino derivatives of 2-methyl-3-aryl-4-quinazolone" XP002138275 cited in the application abstract & IZV. VYSSH. UCHEB. ZAVED., KHIM. KHIM. TEKHNOL. (IVUKAR);1971; VOL.14 (11); PP.1685-9, Perm. Farm. Inst.;Perm; USSR ----</p> <p style="text-align: center;">-/-</p>	1-12

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

° Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

22 May 2000

Date of mailing of the international search report

19. 06. 00

Name and mailing address of the ISA

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Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Scruton-Evans, I

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 00/00912

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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A	HANSON G J: "inhibitors of p38 kinase" EXPERT OPINION ON THERAPEUTIC PATENTS, GB, ASHLEY PUBLICATIONS, vol. 7, no. 7, 1 January 1997 (1997-01-01), pages 729-733, XP002086152 ISSN: 1354-3776 the whole document ----	1-12
P,A	WO 00 07991 A (BROWN GEORGE ROBERT ;ZENECA LTD (GB); BROWN DEARG SUTHERLAND (GB)) 17 February 2000 (2000-02-17) the whole document ----	1-12
A	WO 95 35304 A (MORRIS NATSCHKE SUSAN L ;CHEN XIANNONG (US); DIAZ JOSE LUIS (US);) 28 December 1995 (1995-12-28) the whole document -----	1-12

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 00/00912

Patent document cited in search report	Publication date	Patent family member(s)			Publication date
WO 0007991	A	17-02-2000			NONE
WO 9535304	A	28-12-1995	US	5550132 A	27-08-1996
			AT	186545 T	15-11-1999
			AU	2906795 A	15-01-1996
			CA	2193645 A	28-12-1995
			DE	69513285 D	16-12-1999
			EP	0766691 A	09-04-1997
			FI	965140 A	20-12-1996
			HU	76332 A	28-08-1997
			JP	10509416 T	14-09-1998
			NO	965520 A	21-02-1997
			US	5679684 A	21-10-1997

INTERNATIONAL SEARCH REPORT

Inte: n Application No
PCT/GB 00/00912

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	C07D409/12	C07D409/14	C07D405/14	A61K31/505	A61P43/00

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B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D

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- *&* document member of the same patent family

Date of the actual completion of the international search

22 May 2000

Date of mailing of the international search report

19. 06. 00

Name and mailing address of the ISA

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Authorized officer

Scruton-Evans, I

INTERNATIONAL SEARCH REPORT

Internatinal Application No
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A	WO 95 35304 A (MORRIS NATSCHKE SUSAN L ;CHEN XIANNONG (US); DIAZ JOSE LUIS (US);) 28 December 1995 (1995-12-28) the whole document	1-12

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB 00/00912

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Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

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Remark on Protest

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 00/00912

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
WO 0007991	A	17-02-2000		NONE
WO 9535304	A	28-12-1995	US 5550132 A AT 186545 T AU 2906795 A CA 2193645 A DE 69513285 D EP 0766691 A FI 965140 A HU 76332 A JP 10509416 T NO 965520 A US 5679684 A	27-08-1996 15-11-1999 15-01-1996 28-12-1995 16-12-1999 09-04-1997 20-12-1996 28-08-1997 14-09-1998 21-02-1997 21-10-1997